

The ocular neurons have undergone a primary alteration like the cerebral neurons, both being embryologically related, developed from the same medullary tube of the involuted ectoderm.

The cerebral degenerative progress can be marked by examining the eyes. These are normal at birth; at three months there is a haziness in the macular region, and the picture is complete generally by the sixth month.

The pathology is very satisfactory, but the etiology is still awaiting the genius of a Sachs, a Hirsch, or a Ward Holden.

HISTOLOGICAL EXAMINATION OF THE EYES IN A CASE OF AMAUROTIC FAMILY IDIOCY.¹

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THE eyes upon which we desire to report are from a patient presented by Dr. James H. McKee before the Philadelphia Pediatric Society in June, 1903, the history of which is given in full by Dr. McKee in a preceding article, in the same number of this JOURNAL. The ophthalmoscopic appearances, seen first in March, 1903, were typical of the disease, and are well illustrated by Dr. Buchanan's sketches. Directly in the macular region of each eye there was a horizontally oval, white area, in the centre of which was a sharply defined cherry-red spot. The white area measured about two disks' diameter across, and faded off gradually into the surrounding retina. The fine retinal vessels were not veiled, and ran uninterruptedly across it. The optic nerves were in a condition of white atrophy, the arteries being especially reduced in calibre. Later examinations made by Dr. Buchanan showed a gradual reduction in the size of the white spot, which took the shape of a vertical instead of a horizontal oval, and became grayish in color, while the red spot assumed a brown hue. The lesion did not disappear entirely.

The child died of pneumonia at St. Christopher's Hospital, February 23, 1904, at the age of twenty-nine and one-half months. Permission to perform an autopsy was difficult to obtain, because of religious beliefs, and after eight hours 10 per cent. formalin was injected into each eye, to prevent, if possible, post-mortem changes.

¹ Read before the Section on Ophthalmology of the College of Physicians of Philadelphia, April 19, 1904.

The autopsy was finally made nineteen hours after death. The eye-balls were removed entire; one was placed in 10 per cent. formalin and the other in Müller's fluid. The one placed in formalin was removed after twenty-four hours and hardened in ascending strengths of alcohol until 75 per cent. was reached. It was then divided in a horizontal plane, the section passing through the macular region, in which the discolored area was still visible macroscopically. Portions of the retina in this region were cut out and embedded in paraffin, so that study could be made of the ganglion cells. The other half was embedded in celloidin, and serial sections were cut and stained with hæmatoxylin-eosin, by the Van Gieson method, and with thionin. The eye placed in Müller's fluid, together with the optic chiasm, remained in this solution, with several changes into fresh fluid, for four weeks, and was subsequently hardened in alcohol, bisected, and embedded in celloidin for study of the changes in the optic nerve by the Weigert method.

The sections cut in paraffin pass directly through the macula and fovea centralis. They were stained with a 2 per cent. solution of thionin, for ten minutes, washed in water, differentiated in absolute alcohol, and mounted in xylol balsam. Microscopic examination shows the following conditions: Post-mortem changes are inconspicuous, and no œdema of the retina can be found. The ganglion cells, however, are in an advanced stage of degeneration. Many of them have disappeared completely, so that in the macula, where the cells are ordinarily present in rows of from three to six or even more, only a single, interrupted row can be seen. The cell bodies are so lacking in chromophilic elements, that they can be detected only in the very deeply stained, and slightly differentiated sections. Then the distorted nucleus is seen to be surrounded by a network which represents the framework of the cells. The cell outlines are irregular, in many cases rounded, and without any dendritic process. The Nissl bodies have disappeared entirely. Compared with the cells in the normal retina of a child they are swollen. In many cases the cell body has disappeared, leaving the nucleus alone. Sections of the Müller solution eye, stained by the Weigert method show the swollen cell bodies better, and reveal the presence of closely packed granules in the cell, which stain dark brown. Sketches made by Dr. Buchanan (Fig. 1) illustrate these changes very distinctly.

The retina, as a whole, is thinner than normal, and the thinning seems to be at the expense of each of the layers. The nerve fibre layer is narrower, the ganglion cells are reduced in number, as has been described, and those of the inner and outer nuclear layer, representing respectively the bipolar ganglion cells, and the nuclei of the visual cells, are also fewer than in the normal eye. Many of the former are irregular in outline, and show nuclear degeneration. The inner segments of the rods and cones are preserved,

but the outer segments are degenerated. This degeneration is possibly in part due to post-mortem changes, but not entirely so, as the sections show penetration of this layer, here and there by

FIG. 1.



Degenerated ganglion cells: *A* and *B*, stained with thionin; *C*, stained with Weigert stain.

clumps of the characteristic pigment granules from the retinal pigment layer. In the formalin eye, the retina has remained in place throughout, and the sections of the part removed for paraffin embedding show that the choroid is included with the retina,

FIG. 2.



Photomicrograph of the optic nerve at its entrance to the eyeball, showing entire atrophy of fibres on the nasal side, with some normal fibres on the temporal side. Weigert stain.

although the retina is ordinarily much more easily removed from the choroid than is the choroid from the sclera. In the macular region, the retina, in the celloidin sections, measures 132μ , while

in similar sections from a normal child's eye, hardened and embedded in the same way, it measures 247μ . The retina is therefore reduced almost one-half in thickness, and the adhesion of the retina and choroid, with the pigmentation of the outer layer, show that a decided atrophy, with adhesion between the retina and choroid must have been present during life. The sections of the optic nerve, stained by the Weigert method reveal an entire absence of normal fibres in its temporal half, and a great reduction in those on the nasal side; this part of the nerve, however, shows many normal fibres, as the photo-micrograph (Fig. 2) by Mr. Walmsley at the Pepper Laboratory demonstrates. Sections of the chiasm and optic tract show complete atrophy of all the nerve fibres.

In the 11 cases in which the anatomical examination has been made, the conditions present in the eyes have been recorded in only 5. The first 2 were Kingdon's cases, in which the eyes were examined by Treacher Collins,^{1,2} who found œdema of the retina, especially located in the outer molecular layer, and atrophy of the optic nerves. At the time of these examinations, however, very little attention was paid to the study of the ganglion cells, and nothing is said specifically about their condition. Moreover, in both cases, the eyes were fixed in Müller's solution, so that the retinas were detached from the choroid and exhibited folds in the macular region. Müller's solution was shown to be a poor fixing solution for the retina by Schultze.³ The membrane is inevitably detached, and its elements are distorted by the pulling of the shrinking vitreous humor. Very deceptive pictures of œdema are produced in this way, as is shown in a striking manner by comparison of the eyes in our case. In the formalin eye the retina is in place, and in the celloidin sections, measures 132μ in thickness at the macula; in the Müller solution eye the retina is completely detached, there is decided spacing out of the layers, and it measures 336μ , or nearly three times that of the retina in the fellow eye. On the other hand, formalin does not disguise an existing œdema, as examination of sections of eyes with detachment of the retina or high-grade optic neuritis will prove. We believe, therefore, that the findings of Collins were due in part to the fixing solution used, and to the deceptive appearances caused by the folds in the macular region.

In the third case (Peterson's) examined by Ward A. Holden,⁴ the autopsy was not made until forty hours after death, so that the results were unsatisfactory, owing to the advanced post-mortem changes.

The fourth case (Hirsch's) was also examined by Holden.⁵ He reported enlargement of the ganglion cells, which had become globular and had lost their chromophilic elements. The cells stained by the Weigert method showed coarse, black granules. The cell membrane and the cytotreticulum could be made out under a

$\frac{1}{18}$ immersion, but no Nissl granules were present, and the cell body had the appearance of having had its liquid contents withdrawn, leaving the naked cell framework.

Finally Mohr's⁶ case, published in 1899, in which the eye was fixed in Flemming's chromic-osmic acid solution. Mohr reported oedema of the outer molecular layer, especially of the so-called Henle fibre layer, which makes up the outer portion of this layer, in the region of the yellow spot, a degeneration of the outer segments of the rods and cones, and the formation of a granular substance between the external limiting membrane and the choroid, which measured 380μ in thickness, although the retina itself in this region measured but 70μ . The thickness of the Henle layer was 350μ against 170μ normally found in the adult retina. These conditions Mohr ascribes to oedema, probably caused by angioneurotic disturbances, the result of pathological alterations in the cervical cord. Such a marked thickening of this region, however, if present during life, would be surely evident ophthalmoscopically, and as Higier⁷ observes, if oedema were caused by such alterations in the cervical cord, we would see the same fundus changes in other forms of organic disease such as syringomyelia, amyotrophic lateral sclerosis, cervical spondylitis, etc. Mohr's findings suggest very strongly that the retina was cut obliquely in this situation, and that the marked thickening was due to this fact. He makes no mention of the condition of the ganglion cells, although Holden's results were known to him, as they are mentioned in the summary.

Our examination, therefore, confirms Holden's view that the essential changes in the eyes are degeneration of the ganglion cells of the retina, and of the nerve fibres of the optic nerves and tracts, which are genetically a portion of the central nervous system. The process is in a more advanced stage, but this is what we should expect, as the child lived about eight months longer than did Hirsch's patient, while the disease was first noted at about the ninth or tenth month in each. It seems more reasonable to explain the white area in the fundus as the result of the swollen and degenerated ganglion cells, which are present in much greater numbers in the macular region than elsewhere, than to conceive it as due to oedema of the tissue. As Falkenheim⁸ says, two facts speak against the assumption of an oedema: in the first place the unchanging appearance of the lesion for months, and the absence of any veiling of the finer vessels in the area. Nor would this theory be incompatible with the gradual reduction in size of the area, which was noted in our case by Dr. Buchanan, as the disappearance of the ganglion cells by degeneration would make the spot less conspicuous. What the condition is which causes this intense and widespread degeneration of the nerve cells and fibres, is as yet undetermined. Sachs⁹ was at first of the opinion that it was due to an arrest of development, but he has altered his views, and now believes,¹⁰ with other

investigators that the condition is a true degenerative one, and that it occurs so early in life because of an imperfect development of the nervous system. In other words, he accepts Gowers' term of "abiotrophy" or essential failure of vitality, and thinks that this is present as an inherited condition in these unfortunate cases. This seems to be the best explanation offered, at present, to account for the facts. Why certain children of a family are affected while others remain healthy, and why the children of Jewish parentage are especially liable to the disease, are questions which still remain to be settled.

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A PATHOLOGICAL STUDY OF AMAUROTIC FAMILY IDIOCY.¹

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AMAUROTIC family idiocy is a disease that has been studied especially by American physicians. Falkenheim² after a careful examination of the literature has found 64 cases reported (1901), of these 47 were seen by physicians, 30 cases (24+6) occurred in America, 11 (9+2) in England, and 23 (14+9) on the Continent of Europe.

More recently (1904) Heveroch³ has collected the records of 86 cases, of which 44 occurred in America.

B. Sachs was the first to recognize the clinical symptoms of amaurotic family idiocy, and gave the disease the name by which it is now known. It was subsequently shown that one symptom of

¹ Read in abstract at the meeting of the American Association of Pathologists and Bacteriologists, April, 1904.

² Jahrbuch f. Kinderheilkunde, 1901, p. 123.

³ Abstract in Neurologisches Centralblatt, October 16, 1904, p. 948.